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|---|---|
| WILSON, MICHAEL C | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1632 | |

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/980,381 | ZOGHBI ET AL. | |
| | Examiner | Art Unit | |
| | Michael C. Wilson | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *48 and 55-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48 and 55-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-47, 49-54 have been cancelled. Claims 56 and 57 have been added. Claims 48 and 55-57 are under consideration in the instant office action as they relate to the elected subject matter: nucleic acid sequences encoding a fusion protein comprising an "atonal-associated protein". The species election of an atonal protein was withdrawn in the previous office action.

Applicant's arguments filed 7-1-04 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Priority*

Provisional application 60/176993 (1-19-00) suggested fusion proteins comprising an atonal-associated amino acid sequence but did not teach SEQ ID NO:58 or 70. '060 taught compositions that included a Math1 protein (pg 7, line 21), but did not did not teach the compositions were fusion proteins. Claim 60 of '060 is the "composition of claim 50, wherein Math1 and the receptor-binding domain of a bacterial toxin comprises a fusion protein." Claim 50 of '060 is a "composition comprising a Math1 protein or gene in combination with a delivery vehicle, wherein the delivery vehicle causes a therapeutically effective amount of Math1 to be delivered into a cell. It is not readily apparent that the fusion protein in claim 60 is a Math1 fusion protein or that the Math1 protein is fused with the receptor-binding domain of the bacterial toxin.

As written, it appears that the "receptor-binding domain" of the "bacterial toxin comprises a fusion protein." Therefore, it is not clear that '060 taught Math1 fusion proteins. '060 did not teach SEQ ID NO:58 or 70 as now required in claims 48 and 55 and did not teach the breadth of an atonal-associated protein having at least 80% identity with both SEQ ID NO:58 and 70 as currently claimed.

The priority data in the bibliographic data sheet incorrectly claims priority to 60/147060 instead of 60/137060. A separate request for corrected filing receipt will be required.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in PCT/US00/15410 on 6-1-00. The certified copy was filed 3-6-02.

The effective filing date of the instant claims is 6-1-00, the filing date of US00/15410.

### *Specification*

The amendments to pg 33, line 21, and pg 51, line 14, have been entered.

### *Claim Rejections - 35 USC § 112*

#### *New Matter*

1. Claims 48 and 55-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention for reasons of record.

Claim 48 as newly amended requires a nucleic acid encoding a fusion protein encoding an "atonal-associated" and a "non-atonal-associated" amino acid sequence. The "atonal-associated" protein comprises about 80% identity to SEQ ID NO: 58 and to SEQ ID NO:70. SEQ ID NO:58 is the mouse transcription factor, Math1 (Akazawa, of record, J. Biol. Chem. 1995, Vol. 270, pg 8730-8738). SEQ ID NO:70 is a 10 amino acid sequence of the mouse Math1 transcription factor (AAs 160-180 of the mouse Math1 protein described by Akazawa).

Claim 55 as newly amended is drawn to a composition comprising i) a nucleic acid sequence equivalent in scope to the nucleic acid sequence of claim 48 (but is not dependent upon claim 55), and ii) a delivery vehicle.

The specification as originally filed did not contemplate a nucleic acid sequence encoding a polypeptide that has at least about 80% identity to SEQ ID NO:58 as broadly claimed (48 and 55). Therefore, the phrase is new matter. Applicants point to pg 10, 33 and 52 for support for the claims as newly amended. Applicants' arguments are not persuasive. The specification contemplates treating an animal with a nucleic acid sequence (pg 9, lines 8-13) wherein the nucleic acid sequence "encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58" (pg 10, lines 5-7). Pg 33, line 21, contemplates delivering a transcription factor having at least about 80% identity to SEQ ID NO:70 to a cell in an animal. Pg 52, lines 11-18, contemplates making the proteins into fusion proteins.

Having 80% identity to 20 amino acids of SEQ ID NO:58 as describe on pg 10, lines 5-7, is of a different scope than having 80% identity to the 354 amino acids of SEQ ID NO:58 as claimed. The broader scope claimed was not contemplated in the specification as originally filed.

The specification does not contemplate a nucleic acid sequence encoding a protein that has at least 80% identity to both SEQ ID NO:58 and 70 as newly amended (48 and 55). Therefore, the phrase is new matter. No support for one nucleic acid sequence having both features can be found in the specification as originally filed. The breadth of atonal-associated by the phrase as newly amended cannot be found and representative number of species within the genus cannot be found.

New claim 56 requires the non-atonal-associated amino acid sequence is a protein transduction domain. New claim 57 requires the transduction domain comprises the HIV TAT protein. Applicants argue support is found on pg 10, lines 15-19. Applicants' argument is persuasive. Pg 10, lines 15-19, contemplates using the nucleic acid sequence in combination with a "delivery vehicle" wherein the "vehicle is the receptor-binding domain of a bacterial toxin or any fusion molecule or is a protein transduction domain. In a specific embodiment said protein transduction domain is from the HIV TAT peptide." Pg 10 does not explicitly contemplate the protein transduction domain has been fused with Math1 or is part of a fusion protein. However, pg 108, Example 22, contemplates combining an 11 amino acid "protein transduction domain" of HIV tat protein with atonal protein to make a fusion protein to allow a rapid dispersal into

the nucleus of all cells of the body. Therefore, it is readily apparent that the discussion of transduction domains on pg 10 refers to a fusion protein as described on pg 108.

2. Claims 48 and 55 remain rejected and claims 56 and 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention for reasons of record.

Claim 48 as newly amended requires a nucleic acid encoding a fusion protein encoding an "atonal-associated" and a "non-atonal-associated" amino acid sequence. The "atonal-associated" protein comprises about 80% identity to SEQ ID NO: 58 and to SEQ ID NO:70. SEQ ID NO:58 is the mouse transcription factor, Math1 (Akazawa, of record, J. Biol. Chem. 1995, Vol. 270, pg 8730-8738). SEQ ID NO:70 is a 10 amino acid sequence of the mouse Math1 transcription factor (AAs 160-180 of the mouse Math1 protein described by Akazawa).

Claim 55 as newly amended is drawn to a composition comprising i) a nucleic acid sequence equivalent in scope to the nucleic acid sequence of claim 48 (but is not dependent upon claim 55), and ii) a delivery vehicle.

The rejection regarding "fragments" of atonal proteins (claim 48) has been withdrawn because the phrase has been deleted.

The rejection regarding a nucleic acid sequence encoding an atonal protein that provides a therapeutic effect (claim 55) has been withdrawn because the phrase was deleted from claim 55.

The specification does not contemplate a nucleic acid sequence encoding a polypeptide that has at least about 80% identity to SEQ ID NO:58 as broadly claimed (48 and 55). Therefore, the phrase lacks written description. Applicants point to pg 10, 33 and 52 for support for the claims as newly amended. Applicants' arguments are not persuasive. The specification contemplates treating an animal with a nucleic acid sequence (pg 9, lines 8-13) wherein the nucleic acid sequence "encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58" (pg 10, lines 5-7). Pg 33, line 21, contemplates delivering a transcription factor having at least about 80% identity to SEQ ID NO:70 to a cell in an animal. Pg 52, lines 11-18, contemplates making the proteins into fusion proteins. Having 80% identity to 20 amino acids of SEQ ID NO:58 as describe on pg 10, lines 5-7, is of a different scope than having 80% identity to the 354 amino acids of SEQ ID NO:58 as claimed. The specification does not provide adequate species within the genus to adequately describe the genus.

The specification does not contemplate a nucleic acid sequence encoding a protein that has at least 80% identity to both SEQ ID NO:58 and 70 as newly amended (48 and 55). No species within the genus (a nucleic acid sequence having both features) can be found in the specification as originally filed. Therefore, the composition having such a nucleic acid lacks written description.

New claim 56 requires the non-atonal-associated amino acid sequence is a protein transduction domain. New claim 57 requires the transduction domain comprises the HIV TAT protein. Applicants argue support is found on pg 10, lines 15-19. Applicants' argument is persuasive. Pg 10, lines 15-19, contemplates using the nucleic acid sequence in combination with a "delivery vehicle" wherein the "vehicle is the receptor-binding domain of a bacterial toxin or any fusion molecule or is a protein transduction domain. In a specific embodiment said protein transduction domain is from the HIV TAT peptide." Pg 10 does not explicitly contemplate the protein transduction domain has been fused with Math1 or is part of a fusion protein. However, pg 108, Example 22, contemplates combining an 11 amino acid "protein transduction domain" of HIV tat protein with atonal protein to make a fusion protein to allow a rapid dispersal into the nucleus of all cells of the body. Therefore, it is readily apparent that the discussion of transduction domains on pg 10 refers to a fusion protein as described on pg 108.

However, a nucleic acid sequence encoding a fusion protein comprising any "amino acid sequence that is not an atonal-associated amino acid sequence" in claim 48 does not have support in the specification as originally filed. The specification describes a fusion protein comprising Math1 or Hath1 and a bacterial toxin or a transduction domain on pg 10, lines 15-19, in view of pg 108, Example 22, and in the description of a fusion protein comprising a bacterial toxin or a transduction domain as a delivery vehicle on pg 10, lines 15-19. It would be readily apparent from pg 10, lines 15-19, that transduction domain on pg 108, Example 22, could be replaced with a bacterial toxin. It is noted that pg 72, lines 17-19, states bacterial toxins can be used as delivery

vehicles, such as Exotoxin A, cholera toxin and Ricin toxin. The specification does not suggest any other non-atonal-associated proteins. Bacterial toxins and transduction domains (two species) do not represent any non-atonal associated protein (the genus) as broadly encompassed by the phrase. An adequate written description of a genus of protein requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the proteins themselves. It is not sufficient to define the protein as not atonal proteins because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any such proteins that may be fused with Math1. Naming a genus of proteins as non-atonal-associated proteins, which are generically known to exist, in the absence of knowledge as to specific non-atonal proteins that function when fused to Math1, is not an adequate description of "non-atonal-associated proteins." Rather, it is an attempt to preempt those of skill in the future from fusing proteins other than bacterial toxins or transduction domains to Math1. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

Claim 55 lacks written description for reason in the paragraph above because a composition further comprising a "nucleic acid sequence that is not an atonal-associated nucleic acid sequence" lacks written description.

Claim 55 lacks written description because the specification does not teach any composition comprising atonal-associated and non-atonal-associated nucleic acids as broadly claimed. Pg 10, lines 15-19, in view of pg 108, Example 22, contemplates

combining a Math1 or Hath1 protein with a transduction domain or bacterial toxin. It is readily apparent that a nucleic acid sequence encoding such a fusion protein was required to make such a fusion protein because fusion proteins must be made using a Math1 nucleic acid fused to a TAT HIV nucleic acid. However, the claim encompasses a composition comprising two non-fused nucleic acid sequences, e.g. a plasmid encoding Math1 and a plasmid encoding TAT. The claim does not require a nucleic acid encoding a fusion protein or that the nucleic acid sequences encoding Math1 or TAT encode a fusion protein. The only composition comprising both nucleic acids described in the specification is a composition comprising a nucleic acid encoding a fusion protein comprising Math1 and TAT. Therefore, the composition lacks written description as written.

In conclusion, claiming all nucleic acids that encoding a fusion protein comprising an atonal-associated protein as broadly claimed without contemplating such a breadth, defining the structure or describing the function of such atonal-associated proteins is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

3. Claims 48 and 55 remain rejected and claims 56 and 57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid sequence encoding a fusion protein, said fusion protein comprising a Math1 protein that is at least about 80% identical to SEQ ID NO:58 operably linked to a bacterial toxin

or to a protein transduction domain, does not reasonably provide enablement for a nucleic acid sequence encoding any atonal-associated protein that is at least about 80% identical to SEQ ID NO:58 as broadly claimed, or that is at least about 80% identical to both SEQ ID NO:58 and SEQ ID NO:70 operably linked to a protein transduction domain of HIV tat protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 48 as newly amended requires a nucleic acid encoding a fusion protein encoding an "atonal-associated" and a "non-atonal-associated" amino acid sequence. The "atonal-associated" protein comprises about 80% identity to SEQ ID NO: 58 and to SEQ ID NO:70. SEQ ID NO:58 is the mouse transcription factor, Math1 (Akazawa, of record, J. Biol. Chem. 1995, Vol. 270, pg 8730-8738). SEQ ID NO:70 is a 10 amino acid sequence of the mouse Math1 transcription factor (AAs 160-180 of the mouse Math1 protein described by Akazawa).

Claim 55 as newly amended is drawn to a composition comprising i) a nucleic acid sequence equivalent in scope to the nucleic acid sequence of claim 48 (but is not dependent upon claim 55), and ii) a delivery vehicle.

The rejection regarding a nucleic acid sequence encoding an atonal protein that provides a therapeutic effect (claim 55) has been withdrawn because the phrase was deleted.

The specification does not enable using a nucleic acid sequence encoding a polypeptide that has at least about 80% identity to SEQ ID NO:58 as broadly claimed

(48 and 55). Therefore, the phrase lacks enablement. Applicants point to pg 10, 33 and 52 for support for the claims as newly amended. Applicants' arguments are not persuasive. The specification contemplates treating an animal with a nucleic acid sequence (pg 9, lines 8-13) wherein the nucleic acid sequence "encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58" (pg 10, lines 5-7). Pg 33, line 21, contemplates delivering a transcription factor having at least about 80% identity to SEQ ID NO:70 to a cell in an animal. Pg 52, lines 11-18, contemplates making the proteins into fusion proteins. The specification does not teach that a protein having 80% identity to the 354 amino acids of SEQ ID NO:58 as claimed has the same function as a protein with 80% identity to 20 amino acids of SEQ ID NO:58 as describe on pg 10, lines 5-7, having. The specification does not teach that any protein with at least about 80% identity to SEQ ID NO:58 shares the same function. Without such guidance it would require one of skill undue experimentation to use any nucleic acid sequence encoding a protein that was about 80% identical to SEQ ID NO:58 as broadly claimed as the "atonal-associated" sequence.

The specification does not teach how to use a nucleic acid sequence encoding a fusion protein comprising Math1 and any "amino acid sequence that is not an atonal-associated amino acid sequence" (claim 48) as broadly claimed. The specification describes a fusion protein comprising Math1 or Hath1 and a bacterial toxin or a transduction domain on pg 10, lines 15-19, in view of pg 108, Example 22, and in the description of a fusion protein comprising a bacterial toxin or a transduction domain as a

delivery vehicle on pg 10, lines 15-19. It is noted that pg 72, lines 17-19, states bacterial toxins can be used as delivery vehicles, such as Exotoxin A, cholera toxin and Ricin toxin. The specification does not suggest any other non-atonal-associated proteins. The specification does not teach how to use a fusion protein comprising Math1 and a cytokine, cytokine receptor, antibody, growth hormone, protease, collagenase, etc. The inoperable and unmentioned embodiments encompassed by the claims are innumerable. Without such guidance it would have required one of skill undue experimentation to use a nucleic acid sequence encoding a fusion protein comprising Math1 and any non-atonal-associated protein as claimed.

Claim 55 is not enabled for reason in the paragraph above because a composition further comprising a "nucleic acid sequence that is not an atonal-associated nucleic acid sequence" lacks written description.

In addition, claim 55 encompasses a composition comprising two non-fused nucleic acid sequences, e.g. a plasmid encoding Math1 and a plasmid encoding TAT, together in the same composition. While the specification contemplates fusing a Math1 or Hath1 protein with a transduction domain or bacterial toxin for delivery, the specification does not teach a Math1 protein could be delivered using a transduction domain or bacterial toxin encoded in a separate vector. The composition is not enabled as broadly written. While one of skill could have possibly made a composition comprising DNA encoding each protein separately, the specification does not teach how to use such a composition to deliver the Math1 protein to cells. Without such guidance it would have required one of skill undue experimentation to use two separate nucleic

acid sequences as encompassed by the claim. Therefore, claim 55 should be limited to a composition comprising a nucleic acid sequence encoding a fusion protein comprising an atonal-associated and a non-atonal-associated protein.

4. Claims 48 and 55 remain and claims 56 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection regarding "atonal-associated protein" in claims 48 and 55 has been withdrawn in part in view of the amendments to the claims describing the atonal-associated protein portion.

However, claims 48 and 55 as newly amended remain unclear as they relate to the non-atonal-associated proteins. The claims refer to "an amino acid sequence that is not an atonal-associated amino acid sequence" (claim 48) or a "an additional nucleic acid sequence that is not an atonal-associated sequence" (claim 55); however, it is unclear if the phrases are intended to exclude only atonal proteins or if the phrases exclude both atonal proteins and proteins associated with atonal proteins. Neither interpretation is readily apparent from the definition of "atonal-associated" provided in the specification. The term "atonal-associated" is defined as "any nucleic acid sequence or amino acid sequence which is the *Drosophilae atonal* nucleic acid sequence or amino acid sequence, or is any sequence which is homologous to or has significant sequence similarity to said nucleic acid or amino acid sequence, respectively." Significant sequence similarity means "greater than 25% and can occur

in any region of another sequence." (pg 23, lines 9-15). Applicants' definition is unclear because proteins having 25% homology to a Drosophilae atonal protein would not share essential structures or functions. It is unclear how any protein sharing 25% homology with any drosophilae atonal protein could reasonably be considered "associated" with an atonal protein. It is unclear if some essential structure or function is also required to determine "atonal-associated" proteins. As such, it cannot be determined how to apply such a definition to non-atonal proteins or nucleic acids encompassed by the claims.

The rejection regarding the phrase "desired amino acid sequence" (claim 48) has been withdrawn because the phrase has been deleted.

The rejection regarding the phrase "therapeutically effective amount of atonal-associated nucleic acid sequence" has been withdrawn because the phrase has been deleted.

***Claim Rejections - 35 USC § 102***

The rejection of claims 48 and 55 under 35 U.S.C. 102(a) as being anticipated by Schwarze (Science, Sept. 3, 1999, Vol. 285, pg 1569-1572) has been withdrawn because Schwarze did not teach an amino acid sequence comprising about 80% identity to SEQ ID NO:58 and at least about 80% identity to SEQ ID NO:70.

The rejection of claims 48 and 55 under 35 U.S.C. 102(b) as being anticipated by Schwab (J. Neurosci. Feb 15, 1998, OE (4) pg 1408-1418) has been withdrawn because Schwab did not teach an amino acid sequence comprising about 80% identity to SEQ ID NO:58 and at least about 80% identity to SEQ ID NO:70.

The rejection of claims 48 and 55 under 35 U.S.C. 102(b) as being anticipated by Brown (Development, 1998, Vol. 125, pg 4821-4833) has been withdrawn because the sequence search of SEQ ID NO:58 did not show the Math5 protein taught by Brown had 80% identity to SEQ ID NO:58 as claimed.

***Claim Rejections - 35 USC § 103***

The rejection of claims 48 and 55 under 35 U.S.C. 103(a) as being unpatentable over Brown (Development, 1998, Vol. 125, pg 4821-4833) in view of Schwarze (Science, Sept. 3, 1999, Vol. 285, pg 1569-1572) has been withdrawn because the sequence search of SEQ ID NO:58 did not show the Math5 protein taught by Brown had 80% identity to SEQ ID NO:58.

Claims 48 and 55 remain rejected and new claims 56 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akazawa (J. Biol. Chem., 1995, Vol. 270, No. 15, pg 8730-8738) in view of Schwartze (Science, Sept. 1999, Vol. 285, pg 1569-1572).

Akazawa taught transfecting eukaryotic cells with a vector encoding mouse atonal protein 1 (math1) (pg 8734, col. 2). Math1 is 87.4% identical to SEQ ID NO:58. Amino acids 160-180 of the math1 taught by Akazawa are 100% identical to SEQ ID NO:70. Akazawa did not teach the vector encoded a fusion protein comprising math1.

However, Schwarze taught a nucleic acid sequence encoding β-gal operably linked to an HIV tat protein transduction domain (¶ bridging pg 1569-1570).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to deliver DNA encoding math1 to a cell using a vector as taught by Akazawa using DNA encoding TAT as taught by Schwartze fused to the DNA encoding math1. One of ordinary skill in the art at the time the invention was made would have been motivated to add the DNA encoding TAT to the DNA encoding math1 to dramatically enhance transduction potential in cultured cells (Schwarze, pg 1572, lines 1-4). Fifty proteins ranging in size from 15-120 kD were transduced in a wide variety of human and murine cell types using the HIV tat protein transduction domain (pg 1570, col. 2, lines 12-16).

Applicants argue the structure claimed is not taught by Azakawa, Schwarze or the combination thereof. Applicants' argument is moot because it provides no reasoning and because the nucleic acid encoding math1 taught by Azakawa was 87.4% identical to SEQ ID NO:58 and because amino acids 160-180 of the math1 protein described by Azakawa were 100% identical to SEQ ID NO:70.

Claims 48 and 55-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ben-Arie (Hum. Mol. Genet. 1996, Vol. 5, pg 1207-1216) in view of Schwartze (Science, Sept. 1999, Vol. 285, pg 1569-1572).

Ben-Arie taught transfecting eukaryotic cells with a vector encoding human atonal protein 1 (hath1) (pg 1208, col. 1, 1$^{st}$ partial ¶, ¶ bridging col. 1-2). Hath1 is 100% identical to SEQ ID NO:58. Amino acids 160-180 of the hath1 taught by Ben-Arie

are 100% identical to SEQ ID NO:70. Ben-Arie did not teach the vector encoded a fusion protein comprising math1.

However, Schwarze taught a nucleic acid sequence encoding β-gal operably linked to an HIV tat protein transduction domain (¶ bridging pg 1569-1570).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to deliver DNA encoding hath1 to a cell using a vector as taught by Ben-Arie using DNA encoding TAT as taught by Schwartze fused to the DNA encoding math1. One of ordinary skill in the art at the time the invention was made would have been motivated to add the DNA encoding TAT to the DNA encoding hath1 to dramatically enhance transduction potential in cultured cells (Schwarze, pg 1572, lines 1-4). Fifty proteins ranging in size from 15-120 kD were transduced in a wide variety of human and murine cell types using the HIV tat protein transduction domain (pg 1570, col. 2, lines 12-16).

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

### ***Double Patenting***

Claims 48 and 55-57 of this application conflict with claims 112 and 117 of Application No. 09/585,645. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application.

Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Applicants request to address this issue upon allowance of '645 is considered non-responsive because every rejection must be addressed. In the case of a double patenting rejection, the response should be an argument or a terminal disclaimer. A request to hold the rejection in abeyance is not a response. However, in order to expedite prosecution, this office action has been written instead of a non-compliance letter.

Claims 48 and 55-57 are provisionally rejected under the judicially created doctrine of double patenting over claims 112 and 117 of copending Application No. 09/585,645. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: Claims 112 and 55 both require an atonal-associated nucleic acid sequence in a delivery vehicle that results in delivery of a therapeutically effective amount of atonal-associated nucleic acid sequence into a cell. Claims 117 is dependent upon claim 112 and requires the atonal protein is fused to a protein transduction domain. Claim 117 is a species of claim 48 and 55 in the instant application.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER